

CLAIMS

What is claimed as the invention is:

1. A method of screening a compound for its effect on neural cells or a neural cell activity, comprising:
  - a) combining the compound with a cell population obtained by differentiating primate pluripotent stem (pPS) cells, wherein at least ~60% of cells in the population express A2B5, NCAM, MAP-2, or Nestin;
  - b) determining any change to cells in the population or their activity that results from being combined with the compound; and
  - c) correlating the change with the effect of the compound on neural cells or a neural cell activity.
2. A method of screening a compound for its effect on neural cells or a neural cell activity, comprising:
  - a) combining the compound with a cell population containing cells that have the same genome as an established human embryonic stem (hES) cell line, wherein at least ~60% of cells in the population express A2B5, NCAM, MAP-2, or Nestin;
  - b) determining any change to cells in the population or their activity that results from being combined with the compound; and
  - c) correlating the change with the effect of the compound on neural cells or a neural cell activity.
3. The method of claim 1, comprising determining whether the compound is toxic to cells in the population.
4. The method of claim 1, comprising determining whether the compound affects ability of cells in the population to be maintained in culture.
5. The method of claim 1, comprising determining whether the compound changes neurotransmitter synthesis, release, or uptake by cells in the population.
6. The method of claim 1, comprising determining whether the compound changes electrophysiology of cells in the population.
7. The method of claim 1, wherein the cell population comprises dopaminergic, serotonergic, or cholinergic neurons.
8. The method of claim 1, wherein the cell population comprises sensory or motor neurons.
9. The method of claim 1, wherein the cell population comprises oligodendrocytes or astrocytes.
10. The method of claim 1, wherein the cell population comprises neural progenitor cells.
11. The method of claim 1, wherein the pPS cells are human embryonic stem cells.
12. The method of claim 1, wherein cells in the population have been genetically altered.

13. The method of claim 12, wherein cells in the population have been genetically altered to express telomerase reverse transcriptase.
14. The method of claim 1, wherein at least 30% of the cells have the morphological characteristics of neurons and are NCAM or MAP-2 positive.
15. The method of claim 14, wherein cells in the population having the morphological characteristics of neurons also have at least three of the following characteristics:
- a) at least 60% of the cells show calcium flux when administered acetylcholine;
  - b) at least 60% of the cells show calcium flux when administered GABA;
  - c) at least 10% of the cells show calcium flux when administered norepinephrine;
  - d) at least 60% of the cells show calcium flux when subjected to an external potassium concentration of 50 mM; or
  - e) at least 25% of the cells demonstrate action potentials when subject to stimulation in a whole-cell patch clamp apparatus.
16. The method of claim 1, wherein the cell population has been obtained by differentiating pPS cells in a medium containing at least two ligands that bind growth factor receptors, selected from the group consisting of EGF, bFGF, PDGF, IGF-1, and antibodies to receptors for these ligands.
17. The method of claim 1, wherein the cell population has been obtained by differentiating pPS cells in a medium containing growth factors, sorting the differentiated cells for expression of NCAM or A2B5, and then collecting the sorted cells.
18. The method of claim 1, wherein the cell population has been obtained by culturing progeny of pPS cells in a medium containing an activator of cAMP, a neurotrophic factor (such as nerve growth factor, neurotrophin 3, or brain-derived neurotrophic factor), or a combination thereof.
19. The method of claim 1, comprising providing the cell population with which the compound is subsequently combined.
20. The method of claim 1, comprising differentiating a human embryonic stem cell line to obtain the cell population with which the compound is subsequently combined.